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Predicting post-traumatic stress disorder treatment response in refugees: Multilevel analysis

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Objectives. Given the recent peak in refugee numbers and refugees' high odds of developing post-traumatic stress disorder (PTSD), finding ways to alleviate PTSD in refugees is of vital importance. However, there are major differences in PTSD treatment response between refugees, the determinants of which are largely unknown. This study aimed at improving PTSD treatment for adult refugees by identifying PTSD treatment response predictors.

Design. A prospective longitudinal multilevel modelling design was used to predict PTSD severity scores over time. We analysed data from a randomized controlled trial with pre-, post-, and follow-up measurements of the safety and efficacy of eye movement desensitization and reprocessing and stabilization in asylum seekers and refugees suffering from PTSD.

Methods. Lack of refugee status, comorbid depression, demographic, trauma-related and treatment-related variables were analysed as potential predictors of PTSD treatment outcome. Treatment outcome data from 72 participants were used.

Results. The presence ($B = 6.5$, $p = .03$) and severity ($B = 6.3$, $p < .01$) of a pre-treatment depressive disorder predicted poor treatment response and explained 39% of the variance between individuals.

Conclusions. Refugee patients who suffer from PTSD and severe comorbid depression benefit less from treatment aimed at alleviating PTSD. Results highlight the need for treatment adaptations for PTSD and comorbid severe depression in traumatized refugees, including testing whether initial targeting of severe depressive symptoms increases PTSD treatment effectiveness.

Practitioner points

- There are differences in post-traumatic stress disorder (PTSD) treatment response between traumatized refugees.
- Comorbid depressive disorder and depression severity predict poor PTSD response.
- Refugees with PTSD and severe depression may not benefit from PTSD treatment.
- Targeting comorbid severe depression before PTSD treatment is warranted.
- This study did not correct for multiple hypothesis testing.
- Comorbid depression may differentially impact alternative PTSD treatments.

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Armed conflict and political oppression disrupt lives and force many to flee their home country to look for protection elsewhere. In 2015, forced migration resulted in almost 20 million refugees and asylum seekers worldwide, 3 million of whom resettled in Western countries, and over 1 million new arrivals in asylum application (UN High Commissioner for Refugees (UNHCR), 2015). Pre-migration experiences of physical and psychological violence in their home country, losing home and loved ones, the stresses of forced migration, and post-migration ordeals (e.g., poor socioeconomic status, financial and legal [asylum] insecurities, acculturation issues, daily hassles) may cause or amplify severe psychological distress in refugees and increase their odds of developing post-traumatic stress disorder (PTSD; American Psychiatric Association (APA), 2013; Bogic, Njoku, & Priebe, 2015; Chu, Keller, & Rasmussen, 2013; Knipscheer & Kleber, 2006; Li, Liddell, & Nickerson, 2016; Slobodin & De Jong, 2015; Steel *et al.*, 2009). These circumstances likely contribute to the elevated PTSD prevalence rates of 5–31% among refugees (Fazel, Wheeler, & Danesh, 2005; Lambert & Alhassoon, 2015; Steel *et al.*, 2009), compared to general-population prevalence rates in North America of 4–7% (Kessler, Chiu, Demler, Merikangas, & Walters, 2005), and European rates of 0–7% (Burri & Maercker, 2014). PTSD is known to heavily interfere with refugees' ability to function as individuals, as well as in their families, communities, and society as a whole (Söndergaard & Theorell, 2004). Finding ways to alleviate the burden of PTSD in refugees is therefore of great importance.

Trauma-focused psychotherapy is an effective treatment strategy for refugees with PTSD (Lambert & Alhassoon, 2015). Lambert and Alhassoon reported a large overall treatment effect ($g = 0.91$) for trauma-focused therapy, although there is great variability in the effect sizes between studies with both very small ($g = 0.1$) and large ($g = 2.4$) treatment effects. These heterogeneous treatment effects may be attributed to patient characteristics (differences between study samples), design variations (e.g., choice of questionnaire, intervention and randomization, number of sessions, and control condition used to calculate treatment effect size), and methodological issues (e.g., sample size; Lambert & Alhassoon, 2015; Slobodin & De Jong, 2015). Despite the overall efficacy, a large proportion of treated refugees (18–54%) show no improvement after PTSD treatment (e.g., Stenmark, Guzey, Elbert, & Holen, 2014; Ter Heide, Mooren, Van de Schoot, De Jongh, & Kleber, 2016), highlighting the complexities of PTSD psychotherapy with people from refugee backgrounds.

To optimize treatment response, outcome research would profit from the identification of markers that distinguish between treatment responders and non-responders. Factors that may predict the outcome of PTSD treatment in a range of trauma-affected populations include PTSD onset, childhood trauma, trauma severity, and initial reactions to trauma (Steinert, Hofmann, Leichsenring, & Kruse, 2015). Only a small number of studies however directly examined predictors of treatment response in refugees. One demographic variable (male gender; Stenmark *et al.*, 2014), one migration-related variable (lack of refugee status; Raghavan, Rasmussen, Rosenfeld, & Keller, 2013), two trauma-related variables (abduction history, Betancourt *et al.*, 2012; offender status, Stenmark, Catani, Neuner, Elbert, & Holen, 2013), one coping variable (lack of a firm belief system; Brune *et al.*, 2002), one treatment variable (the number of trauma-focused treatment sessions; Lambert & Alhassoon, 2015), and two clinical variables (comorbid depression, Silove, Manicavasagar, Coello, & Aroche, 2005; poorer pre-intervention mental health, Van Wyk, Schweitzer,

Brough, Vromans, & Murray, 2012) have been found to predict poor treatment response.

In addition to these variables, other variables are often clinically assumed to influence treatment response. Differences in refugee treatment response may be explained by ongoing psychosocial stressors (Miller & Rasmussen, 2010). For example, uncertainty about a refugee status (i.e., having a formal refugee status vs. seeking a formal refugee status as an asylum seeker), accompanied by the fear of forced return to the home country, may reverse any beneficial treatment effects (McFarlane & Kaplan, 2012), whilst status obtainment improved treatment outcome (Raghavan *et al.*, 2013). Language difficulties and the need for an interpreter may also clinically be assumed to diminish treatment response (Miller, Martell, Pazdirek, Caruth, & Lopez, 2005; National Institute for Clinical Excellence (NICE), 2005). Furthermore, the number and nature (civilian, political, veteran) of refugees' traumatic experiences may influence treatment response. Different experiences may have different contextual meanings that could complex symptom constellations and affect treatment outcome (Nickerson, Bryant, Silove, & Steel, 2011). Political activists are regularly subjected to imprisonment for opposing, criticizing, or participating in political activities against the government. They are more likely to face isolation, and physical and mental torture. Unlike political activists, veterans are former members of a State's armed forces; they are more often exposed to combat situations. Civilian refugees, on the other hand, are not active members of the government or any group in conflict with the government. Such experiences shape the social perspective in which PTSD recovery takes place.

The aim of the study was to examine treatment outcome predictors in a sample of treated refugees and asylum seekers with PTSD. The term 'refugee' is used throughout the article to refer to both refugees and asylum seekers. The goal was to investigate novel prospective outcome predictors as well as to replicate previous refugee treatment outcome predictor findings. We conducted a multilevel analysis of PTSD treatment outcome data of adult refugees who participated in a randomized controlled trial (RCT). Multilevel analysis is an advanced statistical method, well suited for analysing longitudinal data with multiple dependent outcomes. Following the available evidence, we hypothesized that pre-treatment PTSD severity, comorbid depression, lack of refugee status, language difficulties (i.e., need for an interpreter during therapy), the number and nature of traumatic events, male gender, fewer psychotherapy sessions, and treatment dropout would predict poorer treatment response.

Methods

Study design

We analysed data from a RCT that compared the safety and efficacy eye movement desensitization and reprocessing (EMDR) and stabilization in asylum seekers and refugees suffering from PTSD. EMDR is a trauma-focused intervention in which a focus on traumatic memories is combined with an attention-demanding task (Shapiro, 2001). Stabilization therapy focuses on building psychosocial skills and competencies, to better cope with or control traumatic distress, improve emotion-regulation, and improve relational skills (Cloitre *et al.*, 2012). The trial was performed at two locations of a Dutch specialist psychotrauma treatment and research centre, Foundation Centrum '45. Both interventions provided 12 hr of treatment contact, divided over nine sessions in the EMDR condition and 12 sessions in the stabilization condition. Participants completed an

assessment at the start of treatment, post-treatment, and at 3-month follow-up. Both treatments were shown to be safe and limitedly efficacious, and no differences in outcomes between treatments were found. For a comprehensive report of study design and outcome, see Ter Heide *et al.* (2016).

Sample

The sample consisted of 72 treatment-seeking adult refugees and asylum seekers who met the DSM-IV-TR diagnostic criteria for PTSD, 36 of whom were assigned to EMDR and 36 to stabilization. Six participants (17%) in the EMDR and 8 (22%) participants in the stabilization condition prematurely terminated treatment. Participants in both conditions benefited equally from treatment (EMDR $\beta = .44$ vs. stabilization $\beta = .48$, $p > .05$). There were no differences in pre-treatment demographic or clinical variables between the two conditions, except that patients in the EMDR condition were more likely to be male (83% vs. 61%; $\chi^2 = 4.4$, $p < .05$). Table 1 provides an overview of the sample characteristics.

The APA ethical standards were followed in the conduct of the study which was approved by the medical ethics committee of the University of Leiden (reference number: OND1324839; ISRCTN20310201). An informed consent was required before patients were included in the study.

Outcome measure

The Clinician-Administered PTSD Scale (CAPS; Blake *et al.*, 1995) served as the primary outcome measure at each measurement interval. It consists of 17 items used to diagnose PTSD according to DSM-IV. Frequency and severity of symptoms are rated on two 5-point Likert scales ranging from 0 (absent) to 4 (extreme), resulting in a score range of 0–136. The CAPS has good psychometric properties across a variety of clinical populations (Weathers, Keane, & Davidson, 2001), including refugees (Charney & Keane, 2007). The internal consistency in the present sample was good (Cronbach's $\alpha = .86$).

Predictive measures

The Hopkins Symptom Checklist (HSCL-25) is a screening instrument for anxiety and depression, which has been designed especially for use with traumatized refugees (Mollica, Wyshak, De Marneffe, Khuon, & Lavelle, 1987). The current study used the depression section of the instrument to assess pre-treatment depression severity. This section consists of 15 items that are rated on a 4-point Likert scale ranging from 1 (not at all) to 4 (extreme). Internal consistency of the depression subscale in the present sample was excellent (Cronbach's $\alpha = .91$). The presence or absence of a DSM-IV diagnosis of comorbid major depressive disorder was routinely assessed at intake by a trained clinician and was also examined as a predictor of treatment outcome.

Data analysis

Independent-samples *t*-tests and chi-square (χ^2) comparisons were used to examine possible differences between patients per condition, after which longitudinal multilevel modelling (MLM) was used to predict PTSD severity scores over time. Longitudinal MLM enables the identification of variables that predict the variance within persons (time level) and between persons (individual level). We calculated the intraclass correlation (ICC)

Table 1. Pre-treatment demographic and clinical characteristics

Sample characteristics	*n* (%)	Mean (*SD*)
Pre-treatment		
Age in years		41.5 (11.3)
Years in the Netherlands[a]		9.4 (5.2)
Region of origin		
Europe	8 (11)	
Asia	20 (28)	
Africa	19 (26)	
Middle East	25 (35)	
Gender		
Male	52 (72)	
Education		
No education/primary school	19 (26)	
Secondary school or higher	53 (74)	
Marital status		
Single/divorced/widow	36 (50)	
Refugee status		
Temporary/permanent permit	59 (82)	
Pending/rejected	13 (18)	
Number of experienced PTEs		12 (5.0)
Type of experienced PTEs		
Murder of friends/family	54 (75)	
Combat situation	48 (67)	
Physical torture[b]	46 (66)	
Imprisonment[b]	44 (63)	
Serious injury[a]	39 (55)	
Rape or sexual abuse[b]	16 (23)	
Refugee background		
Civilian	30 (42)	
Political	17 (24)	
Veteran	10 (14)	
Comorbid depressive disorder	46 (64)	
Symptom severity levels		
PTSD severity		76.5 (18.1)
Depression severity[a]		2.9 (0.56)
Post-treatment		
Interpreter presence	40 (56)	
Number of sessions T1–T2		10.7 (2.8)
Treatment dropout	14 (19)	

Note. PTEs = potentially traumatic events; PTSD = post-traumatic stress disorder.
PTSD severity was measured with the Clinician-Administered PTSD Scale. Depression severity was measured with the HSCL-25.
[a]$n = 71$.
[b]$n = 70$.

statistic to determine which proportion of the total variance is located at each of these levels (Hruschka, Kohrt, & Worthman, 2005). The level-1 variables consisted of PTSD symptom severity at each assessment and included the assessment itself (time). The pre-treatment assessment was considered time = 0. Each subsequent assessment increased

the time variable by 1. Level-2 variables consisted of the between-individual variables to predict changes in the slope of time. MLM does not assume independence between outcome observations nor between the residuals and errors (Graham, 2009). It is better suited than ANOVA repeated measures to deal with assumptions of sphericity, unbalanced data, sampling hierarchy, and missing data, and it increases statistical power beyond ANOVA designs (Hruschka *et al.*, 2005). Classic standard errors were used because robust standard errors may be biased in samples with <100 patients (Hox & Maas, 2001).

To enhance sample size, CAPS severity scores were imputed. We created 10 imputation data sets using predictive mean matching (PMM) and imputed 15% of the post-treatment and 13% of the follow-up CAPS scores. There were no missings in the level-2 data (i.e., individual predictor data), except for one person with a missing pre-treatment HSCL-25 (depression) score. PMM is a recommended multiple imputation technique to increase the reliability of the results (Vink, Frank, Pannekoek, & Van Buuren, 2014). To preserve the multilevel structure of the data and, consequently, precise estimates, a partitioned PMM was used (Vink, Lazendic, & Van Buuren, 2015). Missing data were considered missing at random (MAR) if patients dropped out of treatment without notification, due to travel distance, or due to increase in suicidal ideations. Participants who discontinued treatment for treatment-related reasons were considered not missing at random (NMAR). All NMAR cases had complete data at all measurement intervals.

A stepwise multilevel model was constructed. Longitudinal intercept-only multilevel models tend to overestimate the variance at the time level (within-subject) and underestimate it at the subject level (Hox, 2010). To offer a more realistic model, the time variable was included in the intercept-only model ($CAPS_{ti} = \beta_{00} + \beta_{10} * TIME_{ti} + r_{0i} + r_{1i} * TIME_{ti} + e_{ti}$). First, the intercept-only model with a fixed-effects time component was compared with the intercept-only model with a random-effects time component, to test whether there were individual trajectories between patients in treatment response (random slope), or whether all patients had a similar trajectory (fixed slope). Full maximum likelihood estimates enabled comparisons between the different fit models. A chi-square test based on the difference in deviance between models enabled assessment of the best model fit. The best fit model was chosen as the baseline model. Second, each univariate predictor variable (pre-treatment PTSD severity, comorbid depression diagnosis and severity, refugee status, interpreter presence during therapy, the number and nature of traumatic events, gender, number of psychotherapy sessions, and treatment dropout) was added to the baseline model to test whether these variables predicted PTSD severity change via the time slope. During this step, we controlled for any possible effects from treatment condition and location (Centre 1 and Centre 2) by adding them to the baseline model. As no difference in efficacy between treatments was found in the RCT, we combined patient data of both conditions to increase predictive power. This strategy is recommended, providing treatment condition is added to the model as a control variable (Moons, Royston, Vergouwe, Grobbee, & Altman, 2009). Third, all significant and control predictors were added to the baseline model and simultaneously analysed in a final multilevel model. We also tested for moderator effects between significant treatment predictors and treatment condition to ascertain whether these predictors influenced each condition differently. The proportion of explained variance (R^2) was calculated for the final model (Hox, 2010). SPSS (version 22; IBM Corp., Armonk, NY, USA) was

used to examine possible differences between patients per condition and to generate the imputation data sets. All multilevel analyses (including imputation analyses) were performed in HLM (version 7) software (Scientific Software International, Skokie, IL, USA).

Results

The results section offers a step-by-step overview of the identification process of predictors. Table 2 consists of a correlation matrix of the principal continuous predictors and PTSD outcome measures at each time measurement interval.

Baseline model

The ICC of the fixed time slope baseline model was 0.57, meaning that 57% of the variance of CAPS outcome scores was explained by differences between individuals at the group level. The remaining 43% of the variance was explained by differences within each subject, indicating the extent to which the CAPS scores of an individual tended to vary over time.

We compared the fixed linear time slope baseline model with a random time slope (Table 3). The random time slope model had a significant better fit compared to the fixed linear slope model ($\chi^2 = 14.1$; $p < .001$). This indicated the presence of unexplained between-subject variation in PTSD symptom severity over time and permitted the search for individual characteristics (predictors) to explain this variability. The baseline model showed an average PTSD symptom severity of 75 CAPS points at pre-treatment and a significant 3-point decrease in PTSD symptoms per time interval ($B = 3.0$, $p < .05$).

Baseline model with predictors

The control variables condition and location were added to the baseline model. Each predictor was subsequently added to the 'baseline plus control variables' model in a separate multilevel analysis. Each separate multilevel model has a different average symptom decrease because part of the decrease is explained by the unique predictors in each model.

Table 2. Correlation matrix

		1	2	3	4	5	6
PTSD severity pre-treatment	1	1					
PTSD severity post-treatment	2	.61**	1				
PTSD severity follow-up	3	.47**	.70**	1			
Depression diagnosis pre-treatment	4	.20	.25	.23	1		
Depression severity pre-treatment	5	.56**	.36**	.47**	.06	1	
Number of sessions received	6	.06	−.04	−.14	−.12	−.01	1

Note. PTSD = post-traumatic stress disorder.
PTSD severity was measured with the Clinician-Administered PTSD Scale. Depression severity was measured with the HSCL-25.
*$p < .05$, **$p < .01$.

Table 3. Hierarchical multilevel regression analyses predicting PTSD treatment outcome ($N = 72$)

	Baseline fixed time model (fixed time slope)		Baseline random time model (random time slope)		Multivariate model		Moderator model	
Parameter	*B*	*SE* (*B*)	*B*	*SE* (*B*)	*B*	*SE* (*B*)	*B*	*SE* (*B*)
	Fixed effects							
Intercept	75.0***	2.2	75.0***	2.2	75.***	2.2	75.***	2.2
Level 1 (CAPS severity score at T1, T2, T3)								
Time	−3.0*	1.4	−3.0*	14	−29.9***	7.9	−48.5**	17.4
Level 2 (characteristics)								
Location					6.4*	2.8	5.8*	2.8
Condition					.51	2.6	18.1	14.7
Dep severity					6.3**	2.3	9.4*	3.7
Dep diagnosis					6.5*	2.9	8.4†	4.3
Dep severity × condition							−5.2	4.8
Dep diagnosis × condition							−3.4	5.4
	Random parameters							
σ_e^2 (*SD*)	232.4 (15.2)		189.7 (13.8)		190.2 (13.8)		190.1 (13.6)	
$\sigma_u^2 0$ (*SD*)	306.1 (17.5)***		186.6 (13.7)***		185.9 (13.6)***		186.1 (13.6)***	
$\sigma_u^2 1$ (*SD*)			42.7 (6.5)**		30.5 (5.5)*		27.8 (5.3)*	
−2 log likelihood ratio	1904.8		1890.7		1877.0		1875.0	

Note. CAPS = Clinician-Administered PTSD Scale; Dep = Depression; PTSD = post-traumatic stress disorder. Location: 0 = Centre 1, 1 = Centre 2; Condition: 0 = EMDR, 1 = Stabilization.
Fit difference between baseline models: $\chi^2(14.1, df = 2, p < .001)$; fit difference between baseline random time model and multivariate model $\chi^2(13.7, df = 4, p < .01)$; fit difference between multivariate model and multivariate model with moderators $\chi^2(2.0, df = 2, p > .05)$.
*$p < .05$, **$p < .01$, ***$p < .001$, $^{\dagger}p < .06$.

Mean pre-treatment depression severity ($B = 6.0$, $SE = 2.4$, $p = .02$) predicted poor PTSD treatment response over time. The model had an average PTSD symptom decrease of 22.9, meaning that for each 1-point increase in HSCL depression score (to a maximum of 4), the PTSD CAPS symptom decrease would be 6 points less, with a maximum of 24 points. Patients with maximum depression severity scores would experience a small increase in PTSD severity at post-treatment and follow-up. This indicated that patients with progressively severe levels of depression had progressively less PTSD symptom reduction over time.

Similarly, a diagnosis of major depressive disorder also proved predictive of poor treatment response ($B = 6.0$, $SE = 3.0$, $p = .05$). The average PTSD symptom decrease in this model was 10.7 points, indicating that patients with a major depressive disorder improved less than patients without a major depressive disorder. None of the other predictors (pre-treatment PTSD severity, refugee status, interpreter presence during therapy, the number and nature of traumatic events, gender, number of psychotherapy sessions, and treatment dropout) were significant.

Multivariate model

The multivariate model (Table 3) included all significant and control predictors in the MLM analysis. The equation was as follows:

$$\begin{aligned}\text{CAPS} = {} & \beta_{00} + \beta_{10} * \text{TIME} + \beta_{11} * \text{CONDITION} * \text{TIME} + \beta_{12} * \text{LOCATION} * \text{TIME} \\ & + \beta_{13} * \text{DEPRESSION DIAGNOSIS} * \text{TIME} + \beta_{14} * \text{DEPRESSION SEVERITY} \\ & * \text{TIME} + r_0 + r_1 + e.\end{aligned}$$

The average PTSD severity decreased by 29.9 points over time. This average slope represents patients with neither depression symptoms nor a diagnosis (best case scenario). For each 1-point increase in pre-treatment depression severity, symptom reduction would be 6.3 points less (SE = 2.3, $p < .01$). Patients with a pre-treatment major depressive diagnosis had 6.5 points less PTSD symptom reduction over time (SE = 2.9, $p = .03$). These findings indicate that worst-case scenario, patients with the maximum depression severity score of 4 and a depressive diagnosis, would experience, on average an increase of 3.6 PTSD severity points between pre-treatment and follow-up. Figure 1 shows four different possible trajectories for patients, based on the presence of a depressive disorder and minimum and maximum depression severity.

The multivariate model was further expanded with two moderator variables (Depression diagnosis × Condition and Depression severity × Condition) to examine whether depression impacted treatment outcome differently for EMDR and stabilization (Table 3). There were no significant moderation effects ($p > .05$) and the expanded model did not provide a better fit ($p > .05$), indicating that depression severity and diagnosis exerted similar effects on treatment outcome for both interventions. Based on these results, the multivariate model without moderators was considered the final model.

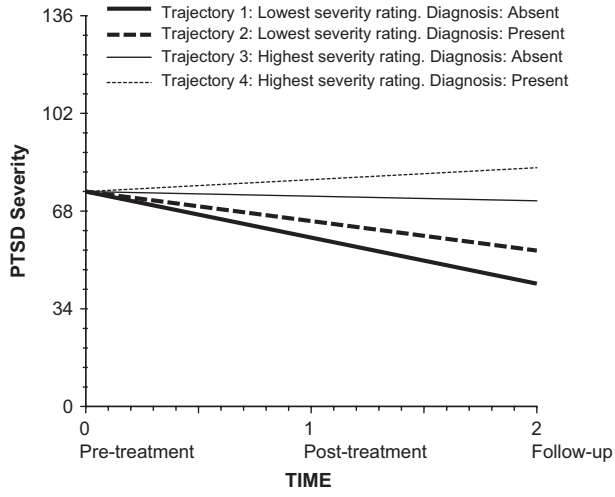

Figure 1. Four treatment trajectories over time. *Note*. The post-traumatic stress disorder (PTSD) severity score (*y*-axis) was measured with the Clinician-Administered PTSD Scale (CAPS). Depression severity was measured with the HSCL-25. The severity rating ranged from 1 (lowest) to 4 (highest). A comorbid depression diagnosis was either Absent (i.e., no comorbid depression) or Present (i.e., a comorbid depression).

The final model explained 39% of the variance between individuals. In sum, the change in PTSD severity scores at post-treatment and follow-up was mostly (57%) the result of individual differences between patients. A sizeable portion (39%) of these differences was explained by the presence and severity of comorbid depression.

Discussion

This study aimed to explain variations in treatment response in an RCT for refugee patients suffering from PTSD. Using multilevel regression analysis at multiple time intervals, the present study identified pre-treatment depressive symptom severity and a diagnosis of depressive disorder as predictors of poor PTSD treatment response. None of the other examined variables predicted treatment response.

Major depressive disorder is frequently associated with PTSD (Buhmann, 2014; Keller, Feeny, & Zoellner, 2014). There is consistent cross-sectional evidence of greater symptom severity, higher disability levels, and poorer functioning among PTSD patients with comorbid depression compared to patients with PTSD only (Bedard-Gilligan *et al.*, 2015; Momartin, Silove, Manicavasagar, & Steel, 2004). Despite this evidence, only one study has considered comorbid depression as a predictor of poor treatment outcome (Silove *et al.*, 2005). Comorbid depression did predict poor PTSD treatment response and premature treatment termination in non-refugee samples, such as traumatized civilians (Bryant, Moulds, Guthrie, Dang, & Nixon, 2003; Taylor *et al.*, 2001) and childhood sexual abuse victims (McDonagh *et al.*, 2005).

The mechanisms through which depression limits psychological recovery are still largely unknown. Angelakis and Nixon (2015) offer several explanations based on emotional processing theory. The first explanation is that successful treatment depends on the modification of traumatic memory structures that underlie emotions, via activation (engagement) of the fear structure through exposure and subsequent habituation. Patients are thus able to emotionally process traumatic memories. An inability to fully experience emotional affect (emotional numbing) in depressed patients may lead to underactivation (underengagement) of the fear structure. Alternatively, depressive patients may be more prone to use transdiagnostic avoidance strategies present in both PTSD and depression, such as rumination and overgeneralizing traumatic memories, which inhibit the full experience of negative emotions. The second explanation is that a greater accessibility of negative autobiographical memories as a result of depression inhibits emotional disengagement from negative trauma content during exposure. This would result in a contrary reaction in which depressive patients become overwhelmed by the emotional intensity of the traumatic memories (overengagement) and successful habituation is prevented.

Angelakis and Nixon based their hypotheses on the assumption that PTSD treatment involves exposure to traumatic memories. Because not all PTSD interventions – for example stabilization – target traumatic memories, we propose alternative hypotheses. In refugee patients with comorbid depression and PTSD, loss and grief may be at the heart of their pathology. The violent loss of friends and family members is a common occurrence among refugees. Refugee patients who experienced a traumatic loss were five times more likely to develop comorbid depression besides PTSD compared to refugee patients without traumatic loss (Momartin *et al.*, 2004). Whilst PTSD development was primarily related to exposure to life-threatening situations (Momartin *et al.*, 2004), comorbid depression development was related to exposure to significant losses (Kersting *et al.*,

2009). Loss may be a major cause of depression, a core aspect of refugee functioning that demands attention besides PTSD, and may require different treatment strategies.

We found no evidence for the predictive value of variables that are traditionally seen as indicative of treatment response in traumatized refugees, including psychosocial stressors (lack of refugee status, language difficulties [need for an interpreter during therapy], nature of the traumatic events), the number of traumatic stressors, gender, and PTSD symptom severity.

Measuring *changes in refugee status* after treatment instead of pre-treatment status may be a more sensitive method to determine the impact of a (lack of) refugee status on treatment outcome. Drožđek, Kamperman, Tol, Knipscheer, and Kleber (2013) reported improved treatment outcome among refugees who gained a refugee status during therapy and argue that removal of status uncertainty increases recovery in the short term; however, a growing awareness of the challenges in rebuilding a future in the host society may again limit these beneficial effects in the long term.

Strengths and limitations

The use of group averages risks masking positive and negative effects between subgroups because it does not account for individual differences in treatment (Moynihan, Henry, & Moons, 2014). Predictor research enables clinicians to identify (non)responders and tailor interventions to optimize response (Riley *et al.*, 2013). The present study is one of the first to examine comorbid depression as a predictor of poor PTSD treatment response in refugees. We used multiple measurements and employed multilevel analysis to better represent the nested data for each individual compared to traditional (ANOVA) methods. The present study examined a severely traumatized patient sample and used an RCT design with few exclusion criteria. Current findings may be applicable to other treatment populations who suffered multiple traumatic events and display high depression comorbidity.

There are also limitations. The present study examined multiple predictors but did not correct for multiple testing and could risk reporting false positives. Due to the lack of predictive studies, a more exploratory analysis was deemed more useful for the detection of possible predictors that would otherwise remain undiscovered if a strictly *a priori* method were used. The current findings need to be replicated. Comorbid depression might have a different effect on alternative PTSD treatments besides EMDR and stabilization, and may not be generalizable to other modalities of PTSD treatment, although the present study moderator analysis showed an equally disruptive effect for two very distinct. The non-significant findings need to be interpreted with caution given the sample size and complexity of the analyses.

Conclusions

Comorbid depression was found to predict poor treatment response. The disorder is highly prevalent among refugees with PTSD (Momartin *et al.*, 2004). In accordance with PTSD NICE (2005) treatment guidelines, we recommend initially targeting severe depression (which will also likely lower PTSD symptoms; Keller *et al.*, 2014), and then only commencing complementary PTSD treatment after alleviation of severe depressive symptoms. There is, however, no evidence available as to whether this sequential approach to treating PTSD and severe depression is superior to treatment of PTSD alone or to a combined PTSD and depression treatment approach (Angelakis

& Nixon, 2015). Clinicians and researchers are urged to examine the impact of treatment timing on PTSD treatment effectiveness for patients with severe comorbid depression.

A sole focus on PTSD for traumatized refugees may fall short in the presence of severe comorbidity (Buhmann, 2014), and may oversimplify complex problems (Briggs & Macleod, 2006). Therapists are recommended to carefully discuss patient needs and whether these primarily focus on PTSD, depression, or perhaps grief. Although an assessment of patient needs is essential in any treatment, it is considered especially so in refugee populations (Summerfield, 1999).

Psychosocial factors that are traditionally assumed to limit treatment response in traumatized refugees, such as lack of refugee status or need for an interpreter, were not found to predict treatment response. These factors warrant further attention regarding their impact on treatment and may imply that practitioners need not refrain from offering psychotherapy for PTSD in refugees based on the assumption that asylum seekers and refugees with little fluency show little treatment response.

In sum, there are major individual differences in treatment response between refugees. The present study identified the presence and severity of a comorbid major depressive disorder as predictors for poor PTSD outcome in traumatized refugees. These results highlight the need for alternative treatment strategies for PTSD and comorbid severe depression in traumatized refugees, including testing whether initial targeting of severe depressive symptoms and only commencing PTSD treatment after reducing depression severity to more moderate levels is more effective than initial PTSD treatment or targeting PTSD and severe depression simultaneously. Future research should determine which approach is superior to alleviate the psychological burden of trauma and displacement in refugees.

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